Cutaneous delayed-type hypersensitivity in patients with atopic dermatitis: Reactivity to topical preservatives

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Background: Patients with atopic dermatitis (AD) have chronic dry skin to which they frequently apply skin care products containing preservatives, and they are predisposed to developing cutaneous delayed-type hypersensitivity.

Objective: We sought to compare the rates of positive patch test reactions to allergens on the North American Contact Dermatitis Group (NACDG) standard tray among patients with and without AD and to assess whether atopic patients in our database were more likely to patch test positive to preservatives.

Methods: A total of 2453 patients underwent patch testing to the NACDG standard screening series. The incidence of positive patch test reaction among patients with AD (n = 342) and without AD (n = 2111) was assessed. Statistical analysis was done using a χ^2 test.

Results: Compared with nonatopic patients, patients with AD were statistically more likely to have positive patch tests. AD was associated with contact hypersensitivity to quaternium-15, imidazolidinyl urea, DMDM hydantoin, and 2-bromo-2-nitropropane-1,3-diol but not to parabens, formaldehyde, or diazolidinyl urea.

Limitations: Only patients suspected of having allergic contact dermatitis were tested. Our population was geographically limited to metropolitan Kansas City, MO, and metropolitan New York City, NY.

Conclusions: Patients with AD should avoid the use of skin care products preserved with formaldehyde releasers. (J Am Acad Dermatol 2014;70:102-7.)

Key words: allergy; atopic eczema; formaldehyde releasers; hypersensitivity; patch testing; preservatives.

Atopic dermatitis (AD), synonymous with atopic eczema, is clinically defined as inflamed, itchy skin that is chronically relapsing.[1] The dry, irritated skin of patients with AD necessitates frequent application of skin care products such as emollients, corticosteroids, and antibacterial creams.[2] In an earlier review of the database used in this study, patients with a history of AD were significantly more likely than nonatopic populations to develop cutaneous delayed-type hypersensitivity (CDTH) to at least 1 allergen on the North American Contact Dermatitis Group (NACDG) standard tray, most significantly to metal allergens including nickel, cobalt chloride, and potassium dichromate.[3]

Abbreviations used:

AD:	atopic dermatitis
CDTH:	cutaneous delayed-type hypersensitivity
NACDG:	North American Contact Dermatitis Group

As a follow-up to this earlier analysis, we were interested in examining 2 areas of study. First we

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wanted to confirm that another year of data from patients patch tested for suspected allergic contact dermatitis supported the conclusion that people with AD are more inclined to have a CDTH reaction than those without AD. Second, we wanted to investigate whether patients with AD are more likely to react to the preservatives paraben mix, formaldehyde, quaternium-15, imidazolidinyl urea, diazolidinyl urea, DMDM hydantoin, and/or 2-bromo-2-nitropropane-1,3-diol, which are all tested on the NACDG standard tray.

CAPSULE SUMMARY

- Atopic individuals have chronic dry skin and are predisposed to developing cutaneous delayed-type hypersensitivity.
- Atopic individuals were significantly more likely to exhibit cutaneous delayed-type hypersensitivity to quaternium-15, imidazolidinyl urea, DMDM hydantoin, and 2-bromo-2-nitropropane-1,3-diol but not to parabens, formaldehyde, or diazolidinyl urea.
- Atopic patients should minimize cutaneous contact with products containing formaldehyde releasers.

METHODS

Between July 1, 1994, and June 3, 2013, a total of 2453 patients, who presented with a clinical suspicion of allergic contact dermatitis, underwent patch testing to the NACDG standard allergen series by the senior author in Kansas City, KS, and New York, NY. Before patch testing, all patients completed a standardized questionnaire regarding demographic, medical, and occupational data. Atopic status (dermatitis, asthma, hay fever) was assessed in all patients; the diagnosis of AD was established using the criteria of Hanifin and Rajka.[4]

Patients were patch tested in a standardized manner using Finn Chamber (Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Bard Medical, Covington, GA).[5] Patch tests were applied to areas of the back free of dermatitis. In general, patients with active dermatitis involving 25% or more of body surface area were not patch tested because of the enhanced possibility of false-positive ("angry back") reactions. Test allergens were purchased from Chemotechnique Diagnostics AB, Malmö, Sweden (1994-2007) or from SmartPractice, Calgary, Alberta, Canada (2008-2013). Allergens were applied on Mondays, and patients were examined at days 2 and 4 after placement. Reactions were assessed based on morphology as previously described.[5] Reactions scored as 1+, 2+, or 3+ were considered a positive allergic response.

All deidentified Health Insurance Portability and Accountability Act–compliant data were entered, retrieved, and evaluated using a computer database (Access 2010, Microsoft Corp, Seattle, WA), and this study was therefore considered exempt from institutional review board approval at Columbia University Medical Center, New York, NY. The incidence of contact sensitization to any allergen, to paraben mix, to formaldehyde, and to formaldehyde releasers (quaternium-15, imidazolidinyl urea, diazolidinyl urea, DMDM hydantoin, and/or 2-bromo-2-nitropropane-1,3-diol) among patients with AD (n = 342) and without AD (n = 2111) was assessed. A χ^2 test was conducted to test whether the difference between observed and expected frequencies was statistically significant, using statistical software (R, Version 3.0.1, R Foundation for Statistical Computing, Vienna, Austria.)

RESULTS

Of the 2453 patients patch tested, 13.94% (n = 342) had a history of AD. Of the 870 males tested, the incidence of AD was 9.20% (n = 80); among the 1581 females, the incidence of AD was 16.57% (n = 262). As seen in Fig 1, among patients with a history of AD, 72.51% had a positive patch test to at least 1 allergen, whereas 64.71% of those with no history of AD had at least 1 positive patch test response ($P = .006$). Subanalysis by gender showed 73.2% of females with a history of AD had a positive patch to at least 1 allergen, whereas 66.3% of females with no history of AD had at least 1 positive patch test response ($P = .032$). Subanalysis for men was not statistically significant, most likely because of the small sample size.

When examining paraben mix and formaldehyde, there was no statistically significant difference in the incidence of positive responses between atopic and nonatopic patients. These results held true when analyzed by gender. However, an interesting finding was that no atopic patients reacted positively to paraben mix (Table I and Fig 2).

Among the formaldehyde releasers, there was a significantly higher incidence of positive patch test reactions to 4 of the 5 releasers analyzed among those persons with a history of AD as compared with the nonatopic population (Table I and Fig 2). For quaternium-15, imidazolidinyl urea, and 2-bromo-2-nitropropane-1,3-diol, patients with AD were statistically more likely to have a positive patch test response than those patients with no history of AD; when analyzed by gender, the above findings held true in women but lost statistical significance in men. For DMDM hydantoin, patients with AD were